United States
Department of
Agriculture

Animal and
Plant Health
Inspection
Service

Program Aid 1580

# Keeping America Free From Foreign Animal Diseases

## Malignant Catarrhal Fever



Volume

5

## Guidelines for Using This Package

This binder contains an integrated suite of educational materials about malignant catarrhal fever. The package can be used in a formal training setting, where a presenter will show the video tape and narrate the slide show using this black-and-white brochure as the script. Or the materials can be used in a self-study program with the reader progressing at his or her own pace.

Within this brochure, readers will notice that certain paragraphs are preceded by a number. These numbers correlate to the slide set. For example, the malignant catarrhal fever slides are marked "MCF" at the top of each plastic slide frame and numbered sequentially from 1 to 50.

If you remove the slides from their protective clear-plastic sleeve (for example, to put them into a carousel for group viewing), please be sure to reposition them in the correct numeric order for the benefit of future users.

This shrink-wrapped suite includes a general and a scientific video tape and a slide set on malignant catarrhal fever and the brochure you are reading now. If your package is incomplete, please contact the following office for replacement materials:

U.S. Department of Agriculture
Animal and Plant Health Inspection Service
Veterinary Services, Emergency Programs
4700 River Road, Unit 41
Riverdale, MD 20737–1231

Instructional packages on other diseases are also available and may be requested by writing to the above address. Titles include
Program Aid 1576 African Horse Sickness
Program Aid 1577 African Swine Fever
Program Aid 1578 Contagious Bovine Pleuropneumonia
Program Aid 1579 Lumpy Skin Disease, Sheep Pox, Goat Pox
Program Aid 1581 Rinderpest, Peste des Petits Ruminants
Program Aid 1582 Vesicular Diseases

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# Malignant Catarrhal Fever

## Definition

1 Malignant catarrhal fever (MCF) is a sporadic, occasionally epizootic, infectious disease of cattle, buffalo, and many species of wild ruminants caused by a herpesvirus. The disease is characterized by low morbidity but high mortality, high fever, catarrhal inflammation of the upper respiratory tract and digestive tract, keratoconjunctivitis, generalized lymphadenopathy, epithelial necrosis in the upper respiratory tract and oral cavity, and dehydration.

Synonyms for MCF are malignant head catarrh, catarrhal fever, and snotsiekte (a South African word meaning "snotting sickness").

## Etiology

2 MCF has historically occurred as two distinct clinicoepidemiologic entities: the alcelaphine (wildebeest, or African) form and the sheep-associated form. The causative agent of the African form—a herpesvirus—was isolated in 1960. Another herpesvirus was reported isolated from sheep-associated MCF in 1977 and 1990. Both forms of MCF are caused by a highly cell-associated lymphotropic herpesvirus in the Gamma subfamily. Two strains of the alcelaphine virus have been recognized: alcelaphine herpesvirus–1 (AHV–1) and alcelaphine herpesvirus–2 (AHV–2). The wildebeest MCF virus (MCFV) belongs to the AHV–1 group. The sheep-associated MCF viruses isolated from cattle in Minnesota and Austria are similar to AHV–1. The sheep associated virus is called ovine herpesvirus–2. AHV–2 is an apathogenic virus that has been isolated from hartebeest and topi.

AHV–1 has been grown in bovine thyroid, kidney, spleen, testis, lung, adrenal and ovine choroid plexus cell cultures. In cultures, this herpesvirus produces syncytia, vacuolation, and type A intranuclear inclusion bodies. The virus in initial passages in cell culture is highly cell associated and can be inactivated by freezing. After adaptation, cell-free virus is produced. AHV–2 grows only in ovine cell cultures.

A viral agent has not yet been isolated from MCF in farmed deer.

The virus is inactivated by lipid solvents and detergents. Cell-free virus will remain viable for at least 30 days at 22 °C if the relative humidity is kept at 100 percent.

## Effective Disinfectants

3 Commonly used disinfectants are effective.

## History

4 The sheep-associated form of MCF was first described in Europe in 1789. The first experimental transmission was done there in 1929 by inoculating cattle with blood collected from a bovine case of sheep-associated MCF.

The wildebeest-associated form of MCF has been recognized by the Masai tribe in Africa for centuries. It was reported in 1850 that Masai observed that MCF occurred when cattle grazed in areas where wildebeest were calving.

MCF has caused the death of many captive wild ruminants in zoos.

## Host Range

5 MCF occurs primarily in domestic cattle (all breeds and ages and both sexes) with highest incidence between 6 months and 4 years of age. Water buffalo and farmed deer can also be affected, the latter having about a 1-percent mortality.

In zoos, MCF has also occurred in many captive wild ruminants: wapiti, red deer, Pere David's, white-tailed deer, white-tailed gnu, white-bearded gnu, gaur, greater kudo, Formosan sika deer, axis deer, nilgai, bison, and banteng.

Reservoir hosts for MCF virus are wildebeest, hartebeest, topi, and domestic and wild sheep. Epidemiologic evidence suggests that the goat may also be a reservoir. When infected, these reservoir animals will develop antibody but show no clinical sign of infection.

Experimental animals in which MCF occurs include rabbits, hamsters, guinea pigs, and rats.

## Geographic Distribution

6 The sheep-associated form of MCF is found worldwide. The alcelaphine (wildebeest) form occurs in Africa and in zoos where susceptible animals are in contact with wildebeest, hartebeest, or topi.

## Transmission and Epidemiology

7 MCF is a disease primarily of domestic cattle, buffalo, farmed deer, and captive wild ruminants. The incidence of MCF is usually sporadic. Morbidity is low, but mortality is high. In the sheep-associated form, cases tend to recur on the same premise over many years, particularly if the sheep or source animal is not removed. However, in recent years there have been a few outbreaks with high (30- to 50-percent) morbidity. In an outbreak in Colorado in the winter of 1971–72, 85 of 231 head of cattle died within 68 days.

In the alcelaphine form of MCF, the virus in the adult reservoir animal is cell associated and thus rarely shed. The Masai believe that cattle become infected when they have contact with placenta from a wildebeest. Virus has not been detected in the placenta, but free virus has been found in the lacrimal and nasal secretion, feces, and hair follicles of neonatal wildebeest from 4 days to 4 months of age.

Passively acquired antibody does not prevent viral replication. The virus has been shown to replicate in the turbinate mucosa and cornea of calves. Transmission to cattle most likely occurs by inhalation of droplets and/or ingestion of the cell-free MCFV on contaminated food or water.

Sheep-associated MCF can occur in cattle when they have close contact with sheep for a long period (e.g., in a stable with common source of feed and water). Most sheep are considered carriers.

In an experiment, three carrier sheep were placed in close contact with cattle. Over a 10-month period, 18 of 50 cattle developed MCF. Cases of MCF continued to develop for 3 to 4 months after the sheep were removed.

There is some evidence that the incidence of MCF in cattle may be higher when ewes are lambing. Cattle are considered to be a dead-end host for MCFV—no horizontal transmission occurs.

## Incubation Period

8 The incubation period for MCF in experimental cases ranges from 7 to 49 days. In natural cases, there is epidemiologic evidence that the incubation period can be as long as 200 days.

## Pathogenesis

9 Exact sites of virus replication are not known. Virus has been isolated from respiratory epithelium and the cornea. Virus appears to infect the large, granular lymphocytes and cause a hyperplasia of "natural killer" (NK) lymphocytes to the extent of resembling neoplasia. The terminal necrotizing lesions are believed to result from an autoimmune phenomenon. In experimental cases, viremia occurs 9 to 17 days after inoculation. The virus in the blood is cell associated (in "mononuclear" cells in the buffy coat).

## Clinical Signs

10 In cattle, there are four clinical forms of MCF:

- Acute form,
- Head and eye form,
- Intestinal form, and
- Mild form.

### Of the Acute Form

11 Some animals, especially deer, die suddenly from MCF. Others may have a fever, severe depression, serous ocular and nasal discharges, enlarged lymph nodes, oral lesions, and diarrhea. Lymph node enlargement is not as prominent as in animals that live longer.

Cattle with the acute form of the disease may have severe inflammation of the oral cavity and nasal mucosa and diarrhea and may die in 1 to 3 days.

### Of the Head and Eye Form

The majority of natural cases of MCF, particularly in cattle, are the head and eye form.

12 Early signs:

- Fever of 104 to 107 °F (40 to 41.6 °C)
- Reddening of the muzzle and serous exudation
- Reddening of the eyes and excessive lacrimation
- Reddening of the oral mucosa
- Enlargement of lymph nodes—generalized lymphadenopathy—particularly evident in the prescapular lymph node

The muzzle and eye lesions in the early stage of MCF are similar to an infection by infectious bovine rhinotracheitis virus.

13 Later signs:

- Reddened areas of epithelium may develop necrosis. Muzzle becomes dry and necrotic. Grey foci in the oral mucosa progress to erosions.
- Buccal papillae become eroded and blunted.
- Mucopurulent exudate in the nostrils
- Mucopurulent exudate from the eyes
- Noisy dyspnea due to obstructed nostrils and trachea—stertor
- Foul odor of the breath due to epithelial necrosis and bacterial growth
- Corneal opacity (usually bilateral) that starts at the limbus and spreads centripetally. The centripetal development of corneal opacity is characteristic of MCF.

- Constipation
- Some animals may have central nervous system signs— excitability, hyperesthesia, convulsions.
- Death occurs 7 to 17 days after the onset of clinical signs.

**Photographs of Clinical Signs**

14 An early sign of MCF: reddening of the eyelids and conjunctivitis.

15 An early sign of MCF: reddening, then drying and cracking of the muzzle.

16 An early sign of MCF: white (necrotic) foci in the nasal epithelium.

17 Classic signs of the head and eye form of MCF: necrosis of the muzzle, slobbering, excessive lacrimation, corneal opacity.

18 Severe case of the head and eye form of MCF: thick nasal exudate, necrotic muzzle, corneal opacity.

19 Erosions of the buccal mucosa.

20 Necrotic epithelium on the muzzle and erosions on the tongue.

21 Enlarged prescapular lymph node.

**Of the Intestinal Form**

22 The intestinal form of MCF will usually have the early signs described for the head and eye form, but the animal dies of severe diarrhea before the latter signs of the head and eye form develop.

The intestinal form may be due to a change in the bacterial flora in the intestinal tract of the infected animal rather than to a direct effect of a viral infection. In an experiment where the MCFV was being passaged in cattle, it consistently caused the head and eye form of the disease; then there were a few animals with the intestinal form. However, with continual passage from these animals, the disease reverted to the head and eye form exclu-

sively. Apparently, the disease allowed the gut flora to cause severe diarrhea, and affected animals died from the diarrhea before the head and eye lesions could develop.

### Of the Mild Form

23 This form of MCF has occurred in cattle inoculated with attenuated viruses. The animals usually recover.

### In Deer and Antelope

24 Clinical signs in deer and antelope species can be less specific than in cattle. Lesions may be minimal, but the following signs may be seen:

- Fever,
- Depression,
- Variable generalized lymphadenopathy,
- Conjunctivitis,
- Moderate corneal opacity (frequently unilateral),
- Serous nasal exudation,
- Oral necrosis,
- Diarrhea, and
- Death.

Lymphoid proliferation is a characteristic of MCF in cervids but may be overlooked because of the hemorrhagic enteritis. As in cattle, the disease in deer and antelope may be sporadic, but cases continually occur in affected herds.

## Gross Lesions

25 & 26

Lesions are most pronounced in the head and eye form of MCF. Lesions are variable, but the following may be observed:

- Muzzle—epithelium is necrotic, and there is a mucopurulent nasal exudate.
- Eye—corneal opacity, mucopurulent conjunctivitis, necrosis of conjunctival epithelium.
- Mouth—epithelial necrosis and/or erosions.
- Lymph nodes and hemolymph nodes—generalized lymphadenopathy (prescapular node may be three or more times normal size; Peyer's patches are prominent due to lymphoid hyperplasia).
- Turbinates—mucopurulent rhinitis.
- Sinuses—mucopurulent sinusitis.
- Larynx—mucopurulent and/or necrotic laryngitis,
- Trachea—mucopurulent tracheitis.
- Lung—focal areas of atelectasis and pneumonia due to inhalation of exudate.
- Liver and kidney—focal areas of lymphoid infiltration (appears almost neoplastic).
- Spleen—may be enlarged; on the cut surface, follicular hyperplasia may be prominent.
- Intestine—mucosa may be reddened. In deer, there may be prominent hemorrhage into the lumen of the lower small intestine, cecum, and colon.
- Urinary bladder—focal areas of edema, erosion, and/or hemorrhage in the mucosa.
- Joints—a fibrinous polyarthritis is not uncommon.

### Photographs of Gross Lesions

27 Greatly enlarged prescapular lymph node compared with a normal node.

28 Erosions on the soft and hard palate.

29 Erosions on the tongue.

30 Necrotic areas in the omasal epithelium.

31 Closeup of necrotic areas in the omasal epithelium.

32 Prominent Peyer's patch—part of the generalized hyperplasia of lymphoid tissue.

33 Multiple erosions of intestinal epithelium and ingesta adhered to foci of necrotic epithelium.

34 The raw-appearing area in the nose is eroded stratified squamous epithelium. There is some exudate on the turbinates and in the nasal passages.

35 Necrotic areas in the larynx.

36 Larynx is covered by a mucopurulent exudate.

37 Mucopurulent exudate in the trachea.

38 Hyperemic, raised, edematous area in the mucosa of the urinary bladder.

39 Hyperplasia of lymph nodules in the spleen.

In the intestinal form, the primary lesion is a very severe enteritis.

## Microscopic Lesions

40 In areas of epithelial necrosis, there is a lymphoid cell infiltrate, vasculitis, and fibrinoid material in the lamina propria.

In lymphoid tissue, there is a loss of small lymphocytes, an infiltration of

macrophages, and a proliferation of large lymphoblastoid cells.

In the liver and kidney, infiltrations of large lymphoblastoid cells may be so severe as to resemble neoplasia.

A characteristic lesion of MCF is a fibrinoid degeneration of arterioles and a lymphoid cell infiltrate in the adventitia. The best areas to examine for vasculitis are the brain, meninges, carotid rete, liver, kidney, adrenal gland, and areas of necrotic epithelium.

### Photomicrographs

41 Necrosis and vacuolation in the stratum spinosum of the tongue.

42 Necrosis of the epithelium in the larynx. Note the cellular infiltrate and fibrinoid material in the lamina propria.

43 Higher magnification of the lamina propria seen in the previous slide.

44 Cellular infiltrate in the lamina propria of the urinary bladder and fibrinoid material in the walls of blood vessels.

## Morbidity and Mortality

45 Morbidity—the number of animals sick at one time—is usually low in MCF. But, over time, the disease may kill many animals. In zoos, MCF has eliminated whole collections of exotic ruminants. Another exception is the outbreak of MCF in Colorado referred to above.

Once an animal develops signs of MCF, mortality approaches 100 percent.

## Diagnosis

### Field Diagnosis

46 MCF should be suspected when an animal has typical clinical signs and lesions. A tentative diagnosis is reinforced if there has been contact with sheep, goat, or alcelaphine antelope.

### Specimens for Laboratory

47 For virus isolation the following specimens should be collected from a moribund animal or immediately after death because the virus is inactivated within an hour after death:

- Blood collected in heparin or EDTA—10 to 20 mL for cell culture inoculation or 300 to 500 mL if cattle are to be inoculated.

- Spleen, lymph nodes, adrenal glands, thyroid glands, and lung.

The specimens should be refrigerated and delivered to the laboratory as quickly as possible. If there is going to be an attempt at virus isolation, it is best to contact the laboratory before collecting the specimens.

**For serology,** collect paired serums. Collect the first sample as soon as possible and the second when the animal is convalescent or moribund.

**For histopathology,** collect pieces of lymph nodes, liver, spleen, kidney, lung, adrenal gland, esophagus, Peyer's patches, urinary bladder, carotid rete, and any lesion in 10-percent formalin.

The brain and eyes should be placed whole in formalin.

### Laboratory Diagnosis

48 **Virus Isolation**—Virus isolation can be attempted using fetal bovine or ovine kidney, thyroid and spleen cell cultures, and/or intraperitoneal inoculation (2 to 5 mL of a 10-percent lymph node suspension) of domestic rabbits or intravenous (500 to 1,000 mL of blood) inoculation of cattle.

The incubation period may be up to 2 months.

Viral isolates are identified by virus neutralization, immunofluorescence, or immunoperoxidase.

Probes have been developed to detect MCFV using the polymerase chain reaction (PCR) technique.

**Serology**—MCF antibody can be detected using virus neutralization, complement fixation, enzyme-linked immunosorbent assay (ELISA), or indirect immunofluorescence. The virus neutralization test is the most specific; antibody to other bovine herpesviruses will cross-react in the other tests.

A single serologic test is of little significance because antibody reacting to MCFV can be present in U.S. cattle.

## Vaccination

49 In experiments, cattle inoculated with attenuated or inactivated MCFV have been resistant to challenge inoculation, but results to date have not been consistent enough to make vaccination practical.

## Control or Eradication

50 Separate susceptible animals from sources of infection (e.g., wild and domestic sheep, goats, and wildebeest), especially when these animals are giving birth.

Zoos introducing wild ruminants that could be carriers of MCFV should consider introducing only serologically negative animals.